Treatment of CLTI after BEST-CLI and BASIL-2: Implications for our practice

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Disclosure

Speaker name: Peter A. Schneider

I have the following potential conflicts of interest to report:

Consulting: Boston Scientific, Surmodics, Silk Road, Medtronic, Cagent, LimFlow, Acotec, Abbott (DSMB)

Enroller in BEST-CLI, committee participant, co-author
BEST-CLI and BASIL-2 Primary Endpoints

Death or major amputation: Bypass 63%; Endo 53%

Death or MALE: Bypass 43%; Endo 57%

Figure 2: Amputation-free survival Kaplan-Meier curve

Bradbury et al. Lancet 2023; Apr 25.
Farber et al. NEJM 2022
<table>
<thead>
<tr>
<th></th>
<th>BEST-CLI (2.7y)</th>
<th>BASIL-2 (40m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endovascular</td>
<td>14.9%</td>
<td>18%</td>
</tr>
<tr>
<td>Bypass</td>
<td>10.7%</td>
<td>20%</td>
</tr>
<tr>
<td>Odds ratio</td>
<td>0.73 (0.54-0.98)</td>
<td>1.23 (0.75-2.01)</td>
</tr>
</tbody>
</table>
BEST-CLI Results in Context

- Death or MALE (above-ankle amputation, new bypass, thrombectomy/thrombolysis, open graft revision)
- Benefit of surgery driven by endo patients converted to bypass.

![Kaplan–Meier Curves of the Primary Outcome and Its Components in Cohort 1.](image)

*Figure 2. Kaplan–Meier Curves of the Primary Outcome and Its Components in Cohort 1.*
Shown is the primary outcome — a composite of major adverse limb events or death from any cause — among patients in the surgical group and the endovascular group in cohort 1 (which included patients who had a single segment of great saphenous vein) (Panel A). The components of the primary outcome were a major index-limb reintervention, including a new bypass graft or graft revision, thrombectomy, or thrombolysis (Panel B); above-ankle amputation of the index limb (Panel C); and death from any cause (Panel D). Shading indicates the 95% confidence interval.

*Farber et al. NEJM 2022*
CD-TLR: typically includes recurrent symptoms, decreased hemodynamics, angiographic evidence of disease.

The technical success of the index procedure was 98% in the surgical group and 85% in the endovascular group. Of the 108 cases of early technical failure in the endovascular group, 66 were treated with a bypass operation within 30 days. The need for and timing of the reintervention was determined by the trial site investigator on the basis of clinical assessment. All first major reinterventions were adjudicated by an independent, multidisciplinary clinical-events committee. A
Technical Success and Evolving Technology

Definition of Technical Failure
Technical failure in the setting of a surgical bypass is defined as occlusion of the bypass graft or failure to achieve a patent bypass graft at the completion of the procedure. Abortion of the procedure prior to successful completion due to non-technical reasons (e.g. due to hemodynamic instability following a myocardial infarction) will still be considered a technical failure of bypass surgery.

Technical failure in the setting of endovascular therapy is defined as the inability to cross a stenosis or occlusion or a residual obstruction of >50% in the superficial femoral artery, popliteal and/ or all tibial arteries (from recoil, dissection, thrombosis, embolization or other complication) such that there is no in-line flow to the foot.

- Evolving technology: Enrollment: 8/14-10/19
- Example: Retrograde access for crossing (antegrade has a 15-20% failure rate).
- Could some of the endo failures be treated with more aggressive endo?
BEST-CLI Results in Context
To which CLTI population does this finding apply?

Anatomic disease morphology

design and implementation. Eligibility was determined locally and varied according to the site and the individual investigator; patients who underwent randomization were those in whom the enrolling team believed there was equipoise between endovascular intervention and bypass surgery. Although the majority of patients (66%) had substantial infrapopliteal-artery involvement, an anticipated future review of angiographic data will elucidate the degree of anatomical complexity among these patients. Because investigators by hemodynamic criteria. Patients were excluded from the trial if they had excessive risk associated with open vascular surgery according to the criteria of the American Heart Association and the American College of Cardiology or according to the medical judgment of the investigator. Details regarding the representativeness of the patient sample are provided in Table S1 in the Supplementary Appendix.12

Fitness for open surgery

Farber et al. NEJM 2022
BEST-CLI Results in Context

The Challenge of Clinical Equipoise

No equipoise when:
- disease morphology is straightforward for endo or
- patient unfit for open surgery.

Selection bias
BEST-CLI Results in Context

Challenge of Clinical Equipoise

- **Fitness for Open Surgery**
- **Disease Morphology**

Easy for Endo | Challenging for endo

- High risk
- Low risk

**Best-CLI Population**

Straightforward endovascular cases and older sicker patients likely excluded.
There is a lot more to learn from BEST-CLI

- NEJM Supplement-61 pages
- WIFI and GLASS sub-segmentation
- Angiographic evaluation of disease morphology-TAP
- Wound healing assessment
- Complications/readmissions/surgical site infection
- QOL
- Cost
- Technical failure of endovascular
BASIL-2 in Context

Death or major amputation: Bypass 63%; Endo 53%

Death: Bypass 53%; Endo 45%
Major Endpoints in BEST-CLI and BASIL-2

<table>
<thead>
<tr>
<th>Mortality</th>
<th>BASIL-2 Perioperative</th>
<th>BEST-CLI Perioperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bypass</td>
<td>6%</td>
<td>1.7%</td>
</tr>
<tr>
<td>Endovascular</td>
<td>3%</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mortality</th>
<th>BASIL-2 at 40 months</th>
<th>BEST-CLI at 2.7 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bypass</td>
<td>53%</td>
<td>33%</td>
</tr>
<tr>
<td>Endovascular</td>
<td>45%</td>
<td>38%</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Major Amputation/Death</th>
<th>BASIL-2 at 40 months</th>
<th>BEST-CLI at 2.7 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bypass</td>
<td>63%</td>
<td>43%</td>
</tr>
<tr>
<td>Endovascular</td>
<td>53%</td>
<td>53%</td>
</tr>
</tbody>
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Key Comparisons: BASIL 2 and BEST CLI

<table>
<thead>
<tr>
<th></th>
<th>BASIL-2</th>
<th>BEST CLI Cohort 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled participants</td>
<td>345</td>
<td>1434</td>
</tr>
<tr>
<td>Age</td>
<td>73</td>
<td>67</td>
</tr>
<tr>
<td>Tissue loss</td>
<td>88%</td>
<td>80%</td>
</tr>
<tr>
<td>Tibial disease</td>
<td>100%</td>
<td>67%</td>
</tr>
<tr>
<td>Endo technical success</td>
<td>87%</td>
<td>85%</td>
</tr>
<tr>
<td>Crossover: endo to bypass</td>
<td>19%</td>
<td>23.5%</td>
</tr>
</tbody>
</table>

BASIL-2 patients are older, probably sicker and with worse disease morphology.

If crossover to bypass had been considered an endpoint event in BASIL-2, the results for bypass and endo would have been much closer.
BEST-CLI and BASIL-2 Results in Context

Challenge of Clinical Equipoise

BASIL-2: older, more tissue loss and ALL had tibial disease.
trial. Although our study and the BEST-CLI trial\textsuperscript{18} were developed, run, and analysed entirely independently, we have collaborated closely with the BEST-CLI trial investigators, and we entered into a data sharing agreement with them before either trial was analysed. The data sharing agreement will allow an in-depth comparison of the two trials that will hopefully explain why some of the outcomes observed appear to be different. One of the outputs will be an individual-patient-level data meta-analysis. Until this work is completed, we can only speculate as to why the two trials appear to have reached different conclusions.
Conclusion

• Endovascular first is appropriate for many, possibly most, but not ALL.

• BEST-CLI: In the studied population, bypass had an advantage.
  • How much advantage is not clear.
  • Additional analyses will give us more direction about which population is best for each treatment strategy.
  • Key unknowns: severity of disease morphology, medical risk of the enrolled patients.

• BASIL-2: In the studied population, endo had an advantage.
  • High mortality in bypass group drove the endpoint.

• BEST-CLI and BASIL-2 were different populations.

• Saphenous vein map and surgical risk assessment applied more liberally.
  • Every CLTI program should ensure it has bypass capability.